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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF: KRÄMER et al.

GROUP: 1617

SERIAL NO: 10/015,550

EXAMINER: Shengjun Wang

FILED: 12/17/2001

FOR: „Use of chroman derivatives in cosmetic or dermatological preparations“

DECLARATION UNDER 37 C.F.R. 1.132**COMMISSIONER FOR PATENTS**

I, Sylke Harenza, Dr. rer. nat., a citizen of Federal Republic of Germany and residing at Ringstr. 13, D-69151 Neckargemünd, Federal Republic of Germany depose and state that:

1. I am a graduate of the University of Heidelberg, Federal Republic of Germany, and received my Ph.D. degree in chemistry in the year 1987.
2. I have been employed by BASF Aktiengesellschaft, D-67056 Ludwigshafen, Germany, for 18 years as a chemist in the field of dyes and pigments (1987-1996) and stabilizers and inhibitors (1996-today).
3. The following experiments were carried out by me or under my direct supervision and control.

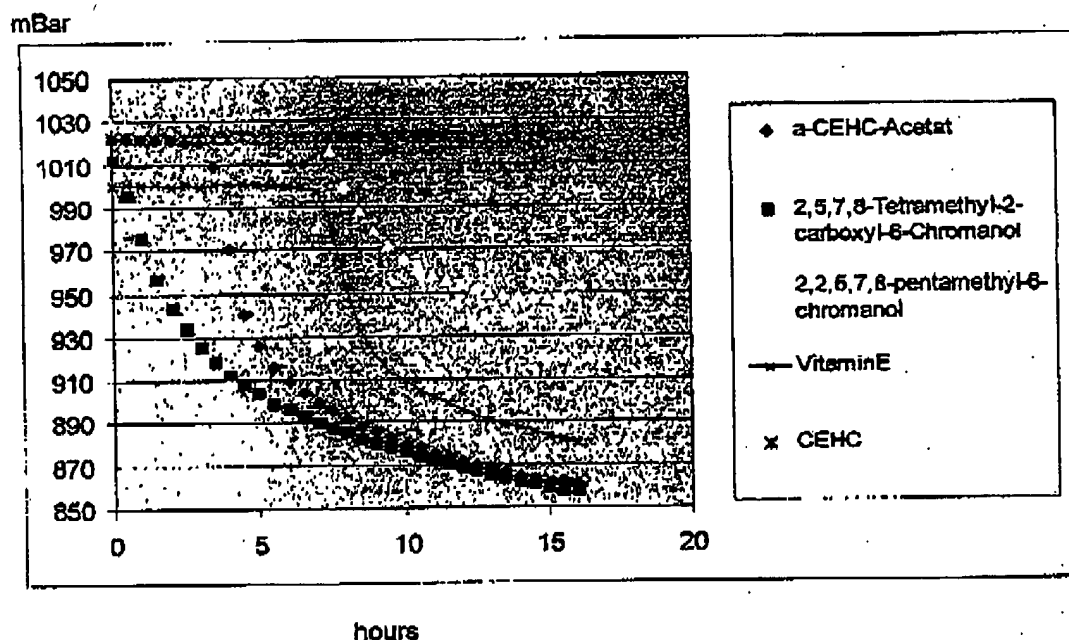
In human body, squalene is produced in the liver and conveyed to skin, where it represents up to 5% of the human-skin fat. Squalene is susceptible to oxidation by atmospheric oxygen. Consequently, a test has been established, the so-called squalene oxidation assay, that is qualified to test the ability of a certain substance to inhibit radical oxidation, particularly to protect the human skin against aging processes due to radical oxidation processes. In this assay the oxidation sensitive compound squalene is incubated in an airtight flask in the presence of oxygen and the test-substance. The flask is connected to a pressure-measuring device. Adding N-Hydroxyphthalimide and Cu-I-chloride to the solution induces the radical oxidation, which is accompanied with a consumption and depletion of oxygen. The decrease in the oxygen concentration in turn is accompanied with a pressure decrease in the flask, determined by the pressure-measuring device. Hence, the pressure decrease within the flask is a function of the radical oxidation of squalene molecules present in the flask.

Consequently, the antioxidative property of a given test-compound is reciprocally proportional to the oxygen consumption/pressure decrease after the induction of the radical oxidation and proportional to the time until an oxygen consumption/pressure decrease can be observed.

Within the scope of this assay the antioxidative activity of the inventive compound α -CEHC (2,5,7,8-Tetramethyl-2(2'-carboxyethyl)-6-chromanol) was compared with substances disclosed by the prior art.

Thus, the antioxidative properties of α -CEHC, α -tocopherol (also known as vitamin E), α -CEHC-acetate, 2,5,7,8-tetramethyl-2-carboxyl-6-chromanol, and 2,2,5,7,8-pentamethyl-6-chromanol were analyzed.

The results are compiled in the following scheme:



Within this experiments, it is evident that α -CEHC is superior to all other substances tested, and the antioxidative properties follow the row α -CEHC > 2,2,5,7,8-pentamethyl-6-chromanol > Vitamin E > α -CEHC-Acetate > 2,5,7,8-Tetramethyl-2-carboxyl-6-chromanol, which doesn't show any protective properties at all. The antioxidative properties of α -CEHC are so strong that there is no sign of an oxidative damage of the test matrix squalene within the timeframe of the assay.

4. I further declare that all statements made herein of my own knowledge are true and that statements made on information or belief are believed to be true; and further that these

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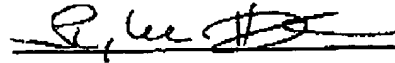
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statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

5. Further deponent saith not.

D-67058 Ludwigshafen, Germany

Place



Signature

23.12.2005

Date

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IN THE UNITED STATES PATENT & TRADEMARK OFFICE**RECEIVED
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IN RE APPLICATION OF: KRÄMER et al.

GROUP: 1617

SERIAL NO: 10/015,559

EXAMINER: Shengjun Wang

FILED: 12/17/2001

FOR: „Use of chroman derivatives in cosmetic or dermatological preparations“

DECLARATION UNDER 37 C.F.R. 1.132**COMMISSIONER FOR PATENTS**

I, Sylke Harenza, Dr. rer. nat., a citizen of Federal Republic of Germany and residing at Ringstr. 13, D-69151 Neckargemünd, Federal Republic of Germany depose and state that:

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3. The following experiments were carried out by me or under my direct supervision and control.

In human body, squalene is produced in the liver and conveyed to skin, where it represents up to 5% of the human-skin fat. Squalene is susceptible to oxidation by atmospheric oxygen. Consequently, a test has been established, the so-called squalene oxidation assay, that is qualified to test the ability of a certain substance to inhibit radical oxidation, particularly to protect the human skin against aging processes due to radical oxidation processes. In this assay the oxidation sensitive compound squalene is incubated in an airtight flask in the presence of oxygen and the test-substance. The flask is connected to a pressure-measuring device. Adding N-Hydroxyphthalimid and Cu-I-chlorid to the solution induces the radical oxidation, which is accompanied with a consumption and depletion of oxygen. The decrease in the oxygen concentration in turn is accompanied with a pressure decrease in the flask, determined by the pressure-measuring device. Hence, the pressure decrease within the flask is a function of the radical oxidation of squalene molecules present in the flask.

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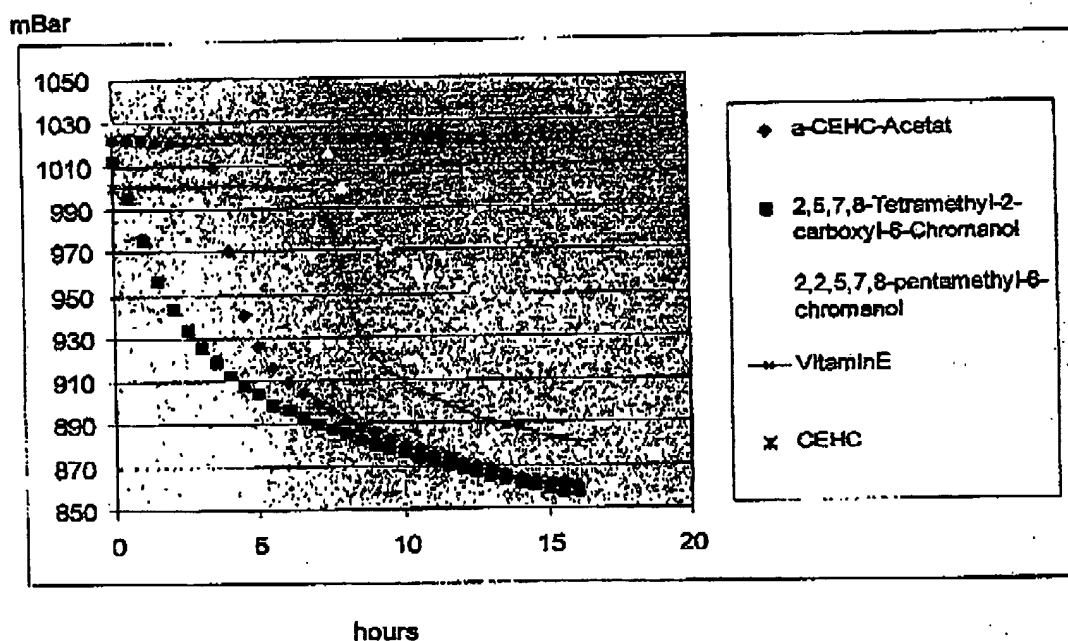
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Consequently, the antioxidative property of a given test-compound is reciprocally proportional to the oxygen consumption/pressure decrease after the induction of the radical oxidation and proportional to the time until an oxygen consumption/pressure decrease can be observed.

Within the scope of this assay the antioxidative activity of the inventive compound α -CEHC (2,5,7,8-Tetramethyl-2(2'-carboxyethyl)-6-chromanol) was compared with substances disclosed by the prior art.

Thus, the antioxidative properties of α -CEHC, α -tocopherol (also known as vitamin E), α -CEHC-acetate, 2,5,7,8-tetramethyl-2-carboxyl-6-chromanol, and 2,2,5,7,8-pentamethyl-6-chromanol were analyzed.

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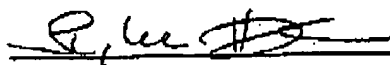
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